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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,512	12/22/2004	Hideakira Yokoyama	2004-1365a	1804

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

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01/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,512	YOKOYAMA ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 49-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 49-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of amendment and remarks filed 9/29/08. Claims 25-37 and 39-48 are canceled. Claim 38 is amended. New claims 49-53 are added.

Rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 112

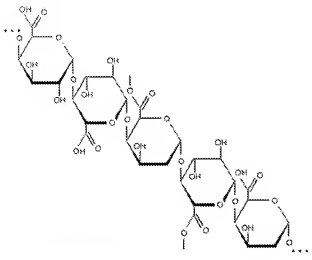
1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

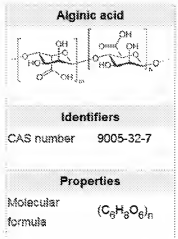
2. Claims 50-53 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

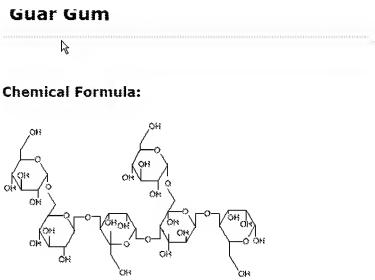
3. Claim 50 depends on claim 38 and further defines the water insoluble polymers, alginic acid or salt, pectin and guar gum as having carboxyl or sulfonic group in the structure of these water soluble polymers. However, as shown below, alginic or alginic salt, pectin and guar gum do not have sulfonic acid functional group. It is thus unclear how these polysaccharides, which have carboxyl groups (pectin and alginic or alginate) and hydroxyl group (guar gum) has sulfonic acid group as directed by instant claims 50, 51 and 52.

Chemical Formula:



PECTIN





Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The cancellation of claims 25-37 and the amendment of claim 38 to specify selection of the water soluble polymers from alginic acid or salt, pectin and guar gum, gives rise to the following new rejections. The requirement in amended claim 38 that the "pH of the preparation" be neutral or basic so as not to dissolve the insoluble alkaline earth metal salt is the property of the preparation; the water-soluble polymer turning into a gel when exposed to the stomach acid is a characteristic of the composition; the breaking stress of the gel is also a property/characteristic of the gel formed in situ.

5. Claims 38 and 49 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bandyopadhyay et al. (US 20020128267).

Bandyopadhyay discloses a pharmaceutical composition (paragraph [0078]) that can be administered orally, intravenously (by injection), intramuscularly, topically, rectally (paragraphs [0086], [0419], [0504]); oral administration is in the form of solid (paragraph [0420]) or liquid (paragraph [0421], [00431]); other routes of administration are parenteral, rectal, topically to the eye (paragraphs [0422]-[0425]). The liquid composition that is administered orally meets the requirement for a liquid composition of the claims and also meets the route of administration, which is oral. In paragraph [0485], Bandyopadhyay specifically describes an embodiment that is an aqueous solution or suspension comprising formulation that gels in situ and comprises excipients (disclosed in US 5,587,175) at about 0.2% to about 3% , the excipients are gellan gum, alginate gum with the alginate gum meeting the requirement for the water soluble polymer;

alkaline earth carbonates or phosphates buffering agents (paragraph [0485]) with these alkaline earth buffering agents meeting the insoluble alkaline earth metal salts. However, while there is a general teaching of oral, topical, rectal, parenteral routes of administration, and while the oral route encompasses solid and liquid forms, and while there is a general teaching that the liquid composition comprise excipient (paragraph [0485]), and while the liquid composition for oral administration may contain wetting agents, suspending agents, sweetening agent and perfuming agents (paragraph [0421]); Bandyopadhyay names calcium carbonate and citrate buffering agents for solid oral dosage form. Therefore, in the alternate, if Bandyopadhyay does not exemplify liquid composition for oral administration to contain calcium carbonate, when the general teaching of Bandyopadhyay is considered as a whole, one having ordinary skill in the art at the time the invention was made would have reasonable expectation that that calcium carbonate buffering agent such as that named for the solid dosage form for oral administration can be incorporated into the liquid dosage to buffer the formulation.

6. Claims 38 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Zatz et al. (US 4,717,713).

Zatz discloses controlled release pharmaceutical composition in the form of a liquid or suspension, with the liquid formulation forming gel-like matrix in the environment of the stomach (abstract; column 2, lines 58-63; column 3, lines 10-26). The composition comprises xanthan gum, sodium alginate or sodium alginate LV (low viscosity calcium depleted), gelatin and carrageenan, methylcellulose and combinations thereof (column 3, lines 27-46), excipients

such as sodium phosphate, calcium phosphate, calcium carbonate, locust bean gum, sodium chloride, sorbitol sugars (column 3, lines 64-68).

Neutral or basic pH of the preparation, the water-soluble polymer turning into a gel when exposed to the stomach acid is a characteristic of the composition and the breaking stress of the gel is also a property/characteristic of the gel formed in situ are all properties of the formulation. A liquid formulation administered by oral route is a route of administration of a formulation. Thus, the liquid pharmaceutical composition of Zatz comprising xanthan gum, sodium alginate or sodium alginate LV (low viscosity calcium depleted), gelatin and carrageenan, methylcellulose and combinations thereof (column 3, lines 27-46), excipients such as sodium phosphate, calcium phosphate, calcium carbonate, locust bean gum, sodium chloride, sorbitol sugars (column 3, lines 64-68) and excipients such as sodium phosphate, calcium phosphate, calcium carbonate, locust bean gum, sodium chloride, sorbitol sugars (column 3, lines 64-68) meet the limitations of claim 38 and 49 with the alginate meeting the water soluble polymer and the carbonate or phosphates in the calcium form meeting the insoluble alkaline earth metal salts.

7. Claims 38, 49-53 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Zatz et al. (US 4,717,713).

Zatz has been described above to anticipate claims 38 and 49. The amount of the sodium alginate in the disclosure of Zatz meeting the limitation of water insoluble polymer is at from about 0.05 to about 3.0 wt.% (column 3, lines 51, 52) and a composition containing about 5 wt.% of calcium carbonate is contemplated (column 4, line 32) with the calcium carbonate and the amount meeting the requirements of the water insoluble alkaline earth metal salts of claims 38, 49-53 in amounts of less than 10% and 5% (claims 50, 51, 52). The difference between claims

50-52 is that Zatz does not specifically say that the molar ratio of the insoluble alkaline earth metal salt to the carboxyl group of the water soluble salt is at 1 to 10 or 3 to 5. But, it would be reasonable to expect that since the amount of the water insoluble alkaline earth metal salt is less than 5% required by these claims, the ratio of the water insoluble alkaline earth metal salt to the carboxyl group of the water soluble polymer would be expected at 3 to 5 as recited and since the amount of the calcium carbonate is about 5%, which is less than 10 and less than 5%, it flows that the ratio in molar amounts of the water insoluble alkaline metal salt to the carboxyl group of the water soluble salt is at the 1 to 10 (claims 50 and 52) or 3 to 5 (claim 51). However, in the alternate, taking the teachings of Zatz, the artisan has the ability of determining the amount of calcium carbonate used in molar amounts in relation to the amount of water soluble polymer and in relation to the molar amount of the carboxyl group of the water soluble polymer. Therefore, it would be prima facie obvious to reasonably expect that using amounts of calcium carbonate or water insoluble alkaline earth metal salt of about 5% meeting the requirements of claims 50-52, a ratio of the metal carbonate to the carboxyl group of the water soluble polymer would be reached that provides the controlled release pharmaceutical composition that gels in the environment of the stomach after oral administration of the liquid pharmaceutical composition.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 38, 49 and 50-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bandyopadhyay et al. (US 20020128267).

11. Bandyopadhyay has been described above to anticipate claim 38 or render claim 38 obvious with calcium carbonate meeting the water insoluble alkaline earth metal salt of claims 49-53 and the alginate meeting the water soluble polymers of claims 38, 50-52. However, Bandyopadhyay is silent on the amounts of the water insoluble alkaline earth metal salts and consequently on the ratio of the metal salt to the carboxyl group of the polymer. But, it is also within the technical skills of the artisan to use amounts of carbonate that would effectively buffer the composition and also determine the amount of the carbonate in relation to the amount of the polymer in molar amounts. Thus, taken the general teachings of Bandyopadhyay, one having ordinary skill in the art at the time the invention was made would have reasonable expectation that calcium carbonate used in amounts appropriate to buffer the formulation would provide formulation that would gel in situ when orally administered for the effective/desired delivery of active agents.

No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Blessing M. Fubara/
Examiner, Art Unit 1618